



Destiny Rezendes @dezzie_rezzie

Dec 21, 2023 · 8 tweets · [dezzie_rezzie/status/1737963752249520306](#)

1 📖 The government MUST release the un-redacted complete Nov. 14, 2023 testimony of Peter Daszak. There must be a comparison between what he said in Nov. & what a set of freshly leaked DARPA proposals reveal.



2 📖 The emails from Daszak [PD] to Baric [RB], Shi, & other EcoHealth [EH] staff on 2/7/2018 all review a draft proposal for DARPA in CoV research. RB may be able to alter viruses w/o being seen but he isn't nearly as skilled with editing grant proposals.

Peter Daszak <daszak@ecohealthalliance.org>

To: Ralph Baric (rbaric@email.unc.edu) <rbaric@email.unc.edu>; Wang Linfa <linfa.wang@duke-nus.edu.sg>; Zhengli Shi (zlishi@wh.iov.cn) <zlishi@wh.iov.cn>; William B. Karesh <karesh@ecohealthalliance.org>; Rocke, Tonie E <trocke@usgs.gov>

Dear All,

Some important points:

- ?!

Luke – please have a go at a first draft of the executive summary slide. I'll pick up from what you've done once you send it to me.

Thanks again to all of you for agreeing to collaborate on this proposal. From what I know of the competition, what DARPA wants, and what we're offering, I think we have an extremely strong team, so I'm looking forward to getting the full proposal together and winning this contract!

Cheers,

Peter

Peter Daszak
President

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EcoHealth Alliance leads cutting-edge research into the critical connections between human and wildlife health and delicate ecosystems. With this science we develop solutions that prevent pandemics and promote conservation.

Abstract Submission Requirements:

- **8 pages with 12 point font or higher (smaller font may be used for figures, tables and charts)
- **Page limit includes all figures, tables, charts and the Executive Summary Slide
- **Copies of all documents submitted must be clearly labeled with the following:
 - DARPA BAA number
 - Proposer Organization
 - Proposal title/Proposal short title
- Submission letter is optional and does not count towards page limit

A. Cover Sheet (does not count towards page limit):

Include the administrative and technical points of contact (name, address, phone, fax, email, lead organization). Also include the BAA number, title of the proposed project, primary subcontractors, estimated cost, duration of project, and the label "ABSTRACT."

B. Executive Summary Slide:

Provide a one slide summary in PowerPoint that effectively and succinctly conveys the main objective, key innovations, expected impact, and other unique aspects of the proposed project. Use the slide template provided at <http://www.fbo.gov>.

****See slide template at bottom of document.**

PROJECT DEFUSE

C. Goals and Impact:

Clearly describe what is being proposed and what difference it will make (qualitatively and quantitatively), including brief answers to the following questions:

1. What is the proposed work attempting to accomplish or do?

We aim to **defuse the potential for emergence of novel bat-origin high-zoonotic risk SARS-related coronaviruses** in Southeast Asia. We envisage a scenario whereby the US warfighter is called on to intervene in a security hotspot in SE Asia for a period of 3-6 months. As planners begin choosing sites for the mission, they will use an app we will design to assess the background risk of a site harboring dangerous zoonotic viruses. If

spillover.

2. How is it done today? And what are the limitations?

Currently, there is no available technology to reduce the risk of exposure to novel coronaviruses from bats, other than avoid the regions where bats harbor these viruses. This includes large areas of southeast Asia where SARS-related CoVs are endemic in bats, which roost in caves during the day, but forage over wide areas at night, shedding virus in their feces and urine. The limitations of this lack of capacity are significant – we have shown evidence of recent spillover of SARS-related CoVs into people in southern China, and have identified viruses in this region that are capable of producing SARS-like illness in humanized mice, with no available vaccines or countermeasures. These viruses are a clear-and-present danger to our military personnel, and to global health security.

3. What is innovative in your approach and how does it compare to current practice and state-of-the-art (SOA)?

****Note: DARPA wants to know, "how the proposed project is revolutionary and how it significantly rises above the current state of the art"**

Our group has shown that bats harbor the highest proportion of potential zoonoses of any mammal group, and that they are able to live with high viral loads due to unique damping of their immune systems, likely as an evolutionary adaptation to flight. We will use this to design strategies to upregulate their immune response in their cave roosts, down-regulate viral replication, and reduce the risk of viral shedding and spillover (immune boosting strategy). At the same time, we will inoculate bats with novel chimeric polyvalent recombinant spike proteins to enhance their immune response against replication of specific, high-risk viruses (immune priming strategy). We will use our innovative modeling to design apps that identify the likelihood of any region harboring high-risk bat viruses. We will design novel, automated approaches to deliver both types of inoculum remotely into caves to reduce exposure risk during decontamination.

4. What are the key technical challenges in your approach and how do you plan to overcome these?

Decide which of following parts to talk about:

3 🇺🇸 They are clear with their intentions stating, "we will inoculate bats with novel chimeric polyvalent recombinant spike proteins to enhance their immune response." they even list "Gain of Function"

Modeling bat suitability

Inventory of caves

Sampling/testing

Reverse engineering, binding assays, mouse expts

Modeling viral risk of evolution and spillover

Modeling inoculation/defusing strategy

Immune modulation

Immune Booster recombinant production

Gain-of-function issue.

Inoculum delivery

Mesocosm expts

Cave expts

5. Who will care and what will the impact be if you are successful?

This will have direct relevance to the warfighter. The potential for deployment to the region in which bat hosts of SARS-related CoVs exist is high – countries include security hotspots (Myanmar, Bangladesh, Pakistan, Lao, Korea). The ability to decontaminate and defuse these viruses will be useful in preventing potentially devastating illness. Furthermore, these technologies, if successful, can be adapted to hosts of other bat-origin CoVs (MERS, SADS), and potentially other zoonotic bat-origin viruses (Hendra, Nipah, EBOV). Finally, our approach is directly applicable to public health measures in the region to reduce the risk of spillover into the general population, as well as for food security by reducing the risk of viruses like SADS-CoV spilling over from bats into intensive pig farms, and devastating and industry, leading to potential civil unrest.

6. How much will it cost and how long will it take?

Will insert this later after calculating and brainstorming.

46 months

Commented [PD1]: Check on the duration of PREEMPT

D. Technical Plan:

Outline and address all technical challenges inherent in the approach and possible solutions for overcoming potential problems. This section should provide appropriate specific milestones (quantitative, if possible) at intermediate stages of the project to demonstrate progress and a brief plan for accomplishment of the milestones.

****Note: "The technical plan should demonstrate a deep understanding of the technical challenges and present a credible (even if risky) plan to achieve the program goal"**

Key Terms/Aspects to Emphasize in Abstract

by DARPA, including genome editing (CRISPR or RNAi), vaccination or DIP bats, in terms of its deployability and scalability. Finally, we will inoculate bats with fragments of non-bat Coronavirus (DETAILS).

Prof. Ralph Baric (UNC) will lead the immune priming work, building on his track record in reverse-engineering and manipulating SARS-CoV, MERS-CoV and other virus spike proteins over the last two decades. He will develop recombinant chimeric spike-proteins (8) based on SARSr-CoVs we have already identified, and those we will discover and characterize during project DEFUSE. RALPH – clearly I didn't really understand the details of your approach. Can you add a couple of paragraphs here and some citations please!

While there are clear advantages to working with fixed populations of cave-dwelling bats, molecule or vaccine delivery is technically challenging. Dr. Tonie Rocke, who developed, trialed, field-tested and rolled out the prairie dog plague vaccine (9), and is currently working on vaccines to bat rabies (10, 11) and white-nose syndrome, will manage a series of experiments in the lab and field to perfect a delivery system for both arms of TA2.

We will conduct initial experiments on a lab colony of wild-caught *Rhinolophus sinicus* bats at Wuhan Institute of Zoology. We (Prof. Wang) have previous experience conducting infection experiments on this bat genus ...(details and citation if possible). First, we will use our recently proven technology to design LIPS assays to the specific high zoonotic-risk SARSr-CoVs (12). We will conduct serological analysis on bats captured for infection experiments, to assess prior exposure to specific strains. These LIPS assays will be made available for use in people to assess exposure of the general population around bat caves in China, and for potential use by the warfighter to assess exposure to SARSr-CoVs during combat missions.

Finally, work on a delivery method will be overseen by Dr. Tonie Rocke at the National Wildlife Health Center who has proven capacity to develop and take animal vaccines through to licensure (9). Using her captive Jamaican fruitbat colony (10, 11), Dr. Rocke will trial out the following strategies for delivery of the molecules, inocula proposed above: 1) aerosolization; 2) transdermally applied nanoparticles; 3) sticky edible spray that bats will groom from each other; 4) automated spray triggered by timers and movement detectors at critical cave entry points.. (Details and ideas please Tonie!). These approaches will then be trialed out on live bats in our three cave sites in Yunnan Province. Fieldwork will be conducted under the auspices of Dr. Rocke, EHA field staff, and Dr. Yunzhi Zhang (Yunnan CDC, Consultant with EcoHealth Alliance). Sections of bat caves will be cordoned off and different application methods trialed out. A small number of bats will be captured and assayed for viral load after treatment, but so as not to disturb the colony, most viral load work will be conducted on fresh fecal pellets

4 🇺🇸 The attempt to lie for \$ is clear; "I do want to stress the US side of this proposal so that DARPA are comfortable w/ our team. Once we get the funds, we can then allocate who does what exact work, & I believe that a lot of these assays can be done in Wuhan." says Daszak

distribution of bat hosts, we have access to biological inventory data on all bat caves in Southern China, as well as information on species distributions across SE Asia from the literature and museum records. We will use radio- and satellite telemetry to identify the home range of each species of bat in the caves, to assess how widely the viral 'plume' could contaminate surrounding regions, and therefore how wide the risk zone is for the warfighter positioned close to bat caves.

We will build environmental niche models using the data above, and environmental and ecological correlates, and traits of cave species communities (eg. phylogenetic and functional diversity), to predict the species composition of bat caves across Southern China, South and SE Asia. We will validate these with data from the current project and data from PREDICT sampling in Thailand, Indonesia, Malaysia and other SE Asian countries. We will then use our unique database of bat host-viral relationships updated from our recent *Nature* paper (1) to assess the likelihood of low- or high-risk SARS-CoVs being present in a cave at any site across the region. At the end of Yr 1, we will use these analyses to produce a prototype app for the warfighter that identifies the likelihood of bats harboring dangerous viral pathogens based on these analyses. The 'high-risk bats near me' app will be updated as new host-viral surveillance data comes on line from our project and others, to ground-truth and fine-tune its predictive capacity. Specifically, our telemetry data on bat movement will be used to assess how often bats from high-risk caves migrate to other colonies and potentially spread their high-risk strains.

The Wuhan Institute of Virology team will conduct viral testing on samples from all bat species in the caves as part of this inventory. Fecal, oral, blood and urogenital samples will be collected from bats using standard capture techniques as we have done for the last decade. In addition, tarps will be laid down in caves to assess the feasibility of surveys using pooled fresh fecal and urine samples. Assays will be designed to correlate viral load in an individual with viral shedding in a fecal sample. Once this is complete, surveys will continue largely on fecal samples so as not to disturb bat colonies and undermine longitudinal sampling capacity. Samples will be tested by PCR and spike proteins of all SARS-related CoVs sequenced. Analyses of phylogeny, recombination events, and further characterization of high-risk viruses (those with spike proteins close to SARS-CoV) will be carried out (REF). Isolation will be attempted on a subset of samples with novel SARS-CoVs. Prof. Ralph Baric, UNC, will reverse engineer spike proteins in his lab to conduct binding assays to human ACE2 (the SARS-CoV receptor). Proteins that bind will then be inserted into SARS-CoV backbones, and inoculated into humanized mice to assess their capacity to cause SARS-like disease, and their ability to be blocked by monoclonal therapies, or vaccines against SARS-CoV (REF).

The modeling team will use these data to build models of 1) risk of viral

Commented [PD3]: Could add " We will continue monitoring the human population proximal to these caves to assess the rates of viral spillover, and ground-truth which specific CoVs are able to infect people

"Once we get the funds we can then allocate who does what exact work and I believe that a lot of these assays can be done in Wuhan.."

Commented [PD4]: Ralph, Zhengli. If we win this contract, I do not propose that all of this work will necessarily be conducted by Ralph, but I do want to stress the US side of this proposal so that DARPA are comfortable with our team. Once we get the funds, we can then allocate who does what exact work, and I believe that a lot of these assays can be done in Wuhan as well...

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Team:

Lead Organization: EcoHealth Alliance, New York

PI: Peter Daszak Ph.D., President & Chief Scientist, EcoHealth Alliance, 3 months/year

Key Personnel:

Billy Karesh DVM, Executive VP for Policy & Health, 1 month/year

Kevin J. Olival Ph.D, VP for Scientific Research, 1 month/year

Jonathan H. Epstein DVM Ph.D., VP for Science & Outreach, 0.5 months/year

Carlos Zambrana-Torrel Ph.D., Assoc. VP for Conservation & Health, 1 month/year

Noam Ross Ph.D., Senior Research Scientist, 2 months/year

Evan Eskew, Research Scientist, 2 months/year

Hongying Li, Program Coordinator, China Programs, 3 months/year

TBD Postdoctoral Researcher modeling and analysis, 12 months/year

TBD Research Assistant, 12 months/year

TBD Program Assistant, 12 months/year

Guangjian Zhu Ph.D., Consultant Field Lead, China Programs, 6 months/year

Yunzhi Zhang Ph.D., Consultant, Yunnan CDC, China, 2 months/year

Subcontract #1: University of North Carolina Medical School

Organizational Lead: Prof. Ralph Baric Ph.D., 2 months/year

XXX

TBD Research Assistant, 12 months/year

Subcontract #2: USGS National Wildlife Health Center

Organizational Lead: Tonie Rocke Ph.D., 2 months/year, no salary requested

TBD Research Technician, 9 months/year

Subcontract #3: Duke NUS, Singapore

Organizational Lead: Prof. Linfa Wang Ph.D., 2 months/year

XXX

TBD Research Assistant, 12 months/year

XXX

Subcontract #4: Wuhan Institute of Virology, China

Organizational Lead: Prof Zhengli Shi Ph.D., 2 months/year

Peng Zhou Ph.D., 2 months/year

TBD Research Assistant, 12 months/year

5 🇺🇸 Methods planned in the draft say "aerosolization" & "transdermally applied Nanoparticle." Baric & Daszak try to downplay Shi/WIVs role in the work despite noting that DARPA would dislike it, & the BSL2 labs in China were handling SARS- a BSL3 selected agent.

ARC - aerosols

William B. Karesh (b) (6) @gmail.com>

Fri 2/2/2018 12:34 PM

To: Roche, Tonie E <trocke@usgs.gov>; Peter Daszak <daszak@ecohealthalliance.org>
Cc: Luke Hamel <hamel@ecohealthalliance.org>

1 attachments (438 KB)
PARC.pdf;



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Palo Alto, CA 94304 USA
+1 650 812 4000
engage@parc.com
www.parc.com

Project Overview

- PARC developed a unique spray technology for large area and high throughput aerosol delivery of highly viscous and concentrated fluids. These fluids can include a range of solutions, e.g., bioactive formulations. This technology has a potential application in large area inoculation of animals/humans with bioengineered formulations for pre-emptive reduction of disease transfer.
- PARC has expertise in fluid/aerosol delivery, leveraging the unique spray method that can aerosolize fluids independent of viscosity or bioactive concentration. This technique enables partners in the biological space to deliver bioactive formulations to animal models with improved chance of efficacy/bioavailability. Potential technical challenges to overcome will be systems integration with rapid development/preparation of pre-emptive agents (potentially with on-demand concentration and composition) and in testing the biological response with animal models.
- PARC can have significant involvement in Technical Area 2 of a PRE-EMPT project: development of a scalable aerosol delivery method for wide-scale inoculation of animal models.

Teaming Overview and Objectives

- PARC has worked with both commercial and university partners for applications of this technology.
- PARC has expertise in fluid delivery, droplet generation, and device and systems integration drawing on our long history with developing printing systems (ink-on-paper). PARC will leverage both previous and on-going work and our related IP portfolio on fluid delivery using platform technologies (spray, transdermal delivery) to meet the PRE-EMPT program objectives.
- PARC has the institutional assets to develop and fabricate new systems for spraying, as well as the background to help improve spray formulation for uptake in mucosal and other targeted membranes.
- PARC is well-positioned to advance its unique spray technology for the PRE-EMPT program, given its demonstrated scalability and wide applicability across different fluids (ranging from low to very high viscosity and independent of bioactive concentration/loading). PARC is looking for collaborators who will investigate disease transmission across animal species and develop the necessary pre-emptive biologicals to prevent such transmission. These engineered biologicals can then be delivered to animal models using the spray technology with maximum chance for efficacy and bioavailability.

Contact Information

Dr. Jerome Unidad; email: Jerome.Unidad@parc.com; telephone: 650-812-4209

by DARPA, including genome editing (CRISPR or RNAi), vaccination or DIP bats, in terms of its deployability and scalability. Finally, we will inoculate bats with fragments of non-bat Coronavirus (DETAILS).

Prof. Ralph Baric (UNC) will lead the immune priming work, building on his track record in reverse-engineering and manipulating SARS-CoV, MERS-CoV and other virus spike proteins over the last two decades. He will develop recombinant chimeric spike-proteins (8) based on SARSr-CoVs we have already identified, and those we will discover and characterize during project DEFUSE. RALPH – clearly I didn't really understand the details of your approach. Can you add a couple of paragraphs here and some citations please!

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We will conduct initial experiments on a lab colony of wild-caught *Rhinolophus sinicus* bats at Wuhan Institute of Zoology. We (Prof. Wang) have previous experience conducting infection experiments on this bat genus ...(details and citation if possible). First, we will use our recently proven technology to design LIPS assays to the specific high zoonotic-risk SARSr-CoVs (12). We will conduct serological analysis on bats captured for infection experiments, to assess prior exposure to specific strains. These LIPS assays will be made available for use in people to assess exposure of the general population around bat caves in China, and for potential use by the warfighter to assess exposure to SARSr-CoVs during combat missions.

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F. If desired, include a brief bibliography

Links to relevant papers, reports, or resumes of key performers.

Do not include more than two resumes as part of the abstract.

****Resumes count against the abstract page limit.**

Commented [PD5]: I'm planning to use my resume and Ralph's. Linfa/Zhengli, I realize your resumes are also very impressive, but I am trying to downplay the non-US focus of this proposal so that DARPA doesn't see this as a negative.

Dr. Peter Daszak is President and Chief Scientist of EcoHealth Alliance, a US-based organization that conducts research and outreach programs on emerging zoonotic diseases. He has published over 300 scientific papers, including the first global map of EID hotspots, strategies to estimate unknown viral diversity in wildlife, predictive models of virus-host relationships, and evidence of the bat origin of SARS-CoV and other emerging viruses. Dr Daszak is Chair of the National Academy of Sciences, Engineering and Medicine's Forum on Microbial Threats and is a member of the Executive Committee and the EHA institutional lead for USAID-EPT-PREDICT. He serves on the NRC Advisory Committee to the USGCRP, the DHS CEEZAD External Advisory Board, and the WHO R&D Blueprint Pathogen Prioritization expert group, and has advised the Director for Medical Preparedness Policy on the White House National Security Staff on global health issues. Dr Daszak won the 2000 CSIRO medal for collaborative research.

Peter Daszak suggested downplaying Linfa & Shi's work on the project to make the proposal seem more American to win the favor of DARPA

Prof. Ralph Baric is a UNC Lineberger Comprehensive Cancer Center member and Professor in the UNC-Chapel Hill Department of Epidemiology. His work focuses on coronaviruses as models to study the genetics of RNA virus transcription, replication, persistence, and cross species transmission. His work crosses the boundaries of microbiology, virology, immunology and epidemiology, looking especially at the population genetics of viruses to find the molecular building blocks for more effective vaccines.

Nipah), which require BSL-4 level facilities for cell culture.

We will use modeling approaches informed by field and experimental data including the data above and other biological and ecological data, to estimate how rapidly high-risk SARS-CoVs will re-colonize a bat population following immune boosting or priming. We will obtain model estimates of the frequency of inoculation required for both approaches, what proportion of a population needs to be reached to have effective viral dampening, and whether specific seasons, or locations within a cave would be most effective to treat. We will then model the efficacy of different delivery methods (spray, swab, cave mouth automated delivery, deliver to specific sections of a cave).

Commented [BRS20]: IN the US, these recombinant SARS CoV are studied under BSL3, not BSL2, especially important for those that are able to bind and replicate in primary human cells. In china, might be growin these virus under bsI2. US reseachers will likely freak out.

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The EHA team and UNC knew that China was doing SARS CoV GoF in inadequate safety level BSLs. When this slipped in the draft it was Ralph Baric [BRS] who reminded Daszak to say BSL3 despite the reality of the lab work in Wuhan because the "US researchers will likely freak out."

Commented [BRS20]: IN the US, these recombinant SARS CoV are studied under BSL3, not BSL2, especially important for those that are able to bind and replicate in primary human cells. In china, might be growin these virus under bsI2. US reseachers will likely freak out.

6 🇺🇸 The plan was to use aerosolized agents to inoculate the bat caves in China, chimerically alter the viruses, enhance them & create biologics. Oh, and also for RBS to try to re-purpose his FAILED Ebola poison, Remdesivir [GS-5734] to use it for CoV [which he later did for Covid-19] 🤔 Also, the undocumented chimera SHC014 cited for use. Daszak's 5+wk old testimony has yet to be released-which begs the question; What else are they hiding? Until our leaders take the initiative, we won't know. People, no, BILLIONS of people have lost; jobs, education, loved ones, livelihoods, freedoms and normalcy for 3 years. There was crimes committed in this pandemic. WE did the hard time..now it's time that the criminals do theirs.

Criminal Intent is apparent here where the suggestion is made to downplay the heavy involvement of WIV in order to “get the funds” of which DARPA would be more inclined to dish out to a familiar team, i.e Americans

urine samples. Assays will be designed to correlate viral load in an individual with viral shedding in a fecal sample. Once this is complete, surveys will continue largely on fecal samples so as not to disturb bat colonies and undermine longitudinal sampling capacity. Samples will be tested by PCR and spike proteins of all SARS-related CoVs sequenced. Analyses of phylogeny, recombination events, and further characterization of high-risk viruses (those with spike proteins close to SARS-CoV) will be carried out (REF). Isolation will be attempted on a subset of samples with novel SARSr-CoVs. Prof. Ralph Baric, UNC, will reverse engineer spike proteins in his lab to conduct binding assays to human ACE2 (the SARS-CoV receptor). **Their group have also devised new strategies to culture SARS-like bat coronaviruses, allowing biological characterization of both high risk strains that can replicate in primary human cells and low risk strains that can only replicate in the presence of exogenous enhancers. Viral spike glycoproteins that bind receptor will then be inserted into SARS-CoV backbones, and inoculated into human cells and humanized mice to assess their capacity to cause SARS-like disease, and their ability to be blocked by monoclonal therapies, or vaccines against SARS-CoV ((PMCS5798318, PMCS567817, PMCS380844, PMCS5578707, PMC4801244, PMC4797993). The Baric group has also demonstrated that a nucleoside analogue inhibitor, GS-5734 (Gilead Inc.) blocks epidemic, preepidemic and zoonotic SARS-CoV and SARS-like bat coronavirus replication in primary human airway cells and in mice (PMC5567817). Consequently, they will evaluate the ability of this drug to block replication of newly discovered pre-epidemic and zoonotic high risk strains. As the drug has been used to effectively treat Ebola virus infected patients (PMC4967715, PMC5583641) as well and has potent activity against Nipah and Hendra viruses (PMC5338263), an alternative intervention for military personnel is prophylactic treatment prior to deployment into high risk settings.**

This massive detail is on the draft of the proposal and excluded from the final proposal

Commented [PD18]: Ralph, Zhengli. If we win this contract, I do not propose that all of this work will necessarily be conducted by Ralph, but I do want to stress the US side of this proposal so that DARPA are comfortable with our team. Once we get the funds, we can then allocate who does what exact work, and I believe that a lot of these assays can be done in Wuhan as well...

Commented [J19]: Can we culture any bat coronaviruses? It might be good to broaden this so we can include novel beta CoVs that we may discover which look like they may be transmissible to people

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Already we see Baric pushing his FAILED Ebola drug and subsequent “kiss of death” covid-19 protocol, Remdesivir

specific, suggesting that they are important in viruses/bats coexistence, and supported by our own work showing that a mutant bat STING restores antiviral functionality (3). By identifying small molecules to directly activate downstream of STING, we have chance to activate bat interferon and then help bats to clear viruses. Similar strategy applies to ssRNA-TLR7 dependent pathways. We will also attempt to boost bat IFN by activating functional bat IFN production pathways. **We will investigate if there are other IFN production pathways in bats. We then boost bat immune responses by ligands specifically to these pathways, e.g. poly(I:C) to TLR3-IFN pathway or 5'ppp-dsRNA to RIG-I-IFN pathway.** A similar strategy has been tested successful in mouse model for SARS-CoV, IAV or HBV (6, 7). We believe treating wild bats with IFN-modulating small molecules by spraying is superior to other invasive strategies that might be considered by DARPA, including genome editing (CRISPR or RNAi), **vaccination** or DIP bats, in terms of its deployability and scalability. Finally, we will inoculate bats with fragments of non-bat Coronavirus (**DETAILS**).

Prof. Ralph Baric (UNC) will lead the immune priming work, building on his track record in reverse-engineering and manipulating SARS-CoV, MERS-CoV and other virus spike proteins over the last two decades. He will develop recombinant chimeric spike-proteins (8) based on SARSr-CoVs we have already identified, and those we will discover and characterize during project DEFUSE. **RALPH – clearly I didn't really understand the details of your approach. Can you add a couple of paragraphs here and some citations please!**

One of the candidates proposed was the unverified SHC014 chimera...

immunity.

Commented [J28]: Agree with Ralph – and this mechanism of delivery would probably be the same for vaccination attempts (intranasal or oral via grooming droplets from fur).

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Commented [BR529]: The structure of the SARS-CoV spike glycoprotein has been solved and the addition of two proline residues at positions V1060P and L1061P stabilize the prefusion state of the trimer, including key neutralizing epitopes in the receptor binding domain (PMC5584442). In parallel, the spike trimers or the receptor binding domain can be incorporated into alphavirus vectored or nanoparticle vaccines for delivery, either as aerosols, in baits, or as large droplet delivery vehicles (PMC4058772, PMC5423355, PMC2883479, PMC5578707, PMC3014161). Initially, we will test various delivery vehicles in controlled conditions in bats in a laboratory setting, taking the best candidate forward for testing in the field.

The Baric laboratory has built recombinant S spike glycoproteins harboring structurally defined domains from SARS epidemic strains, pre-epidemic strains like SHC014 and zoonotic strains like HKU3. It is anticipated that recombinant S glycoprotein based vaccines harboring immunogenic blocks across the group 2B coronaviruses will induce broad based immune responses that simultaneously reduce genetically heterogeneous virus burdens in bats, thereby reducing disease risk (and transmission risk to people) in these animals for multiple years (PMC3977350, PMC2588415).

Source : https://usrtk.org/wp-content/uploads/2023/12/2021-006245-Combined-Records_Redacted-1-235.pdf

@threadreaderapp unroll

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